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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/773,866	02/01/2001	David Thomas	PNJ-001	3286

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DARBY & DARBY
ATTN: PAUL F. FEHLNER, PH.D
805 THIRD AVE.
NEW YORK, NY 10022

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/773,866	THOMAS ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-24 and 29-48* is/are pending in the application.

4a) Of the above claim(s) *33-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24 and 29-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 10/12/05 has been entered.

Applicant's amendment, filed 10/12/05, has been entered.
Claims 21-24 and 29-30 have been amended.
Claims 31-48 have been added.
Claims 1-20 and 25-28 have been canceled previously.

Newly submitted claims 33-48 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Newly submitted claims are drawn to CD40-specific antibodies and hybridomas not presented in the previous RCE submission. CD40-specific antibodies are related to methods of enhancing CTL responses with CD40-specific antibodies as product and process. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. 806.05(h)).

In the instant case, the antibody products as claimed can be used in a materially different process such as affinity purification and detection assays. Also, a number of agents and antigens can be used to stimulate CTL responses, other than the use of CD40-specific antibodies. Therefore, they are patentably distinct.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 33-48 are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03.

Claims 21-24 and 29-32 are being acted upon as they read on applicant's previous claimed invention.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Action will be in response to applicant's amendment, filed 10/12/05.

The rejections of record can be found in previous Office Action, mailed 7/12/05.

3. Applicant's amendment to the specification, filed 10/12/05, concerning the deposit information of the disclosed and claimed antibodies / hybridomas is acknowledged.

As noted above, the claims being acted upon do not recite the specific antibodies.

However, if claims drawn to the particular antibodies recited in claim 33 were introduced into the method claims, then applicant is reminded of the following.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

4. The previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter with respect to the recitation of "for enhancing a pre-existing immune response", "contacting" and "without completely blocking" has been withdrawn given applicant's amended claims, filed 10/12/05.

5. Claims 21-24 and 29-32 are rejected under 35 U.S.C.§ 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed:

"wherein said anti-CD40 antibody or binding fragment is capable of blocking binding of CD40L on a human T lymphocyte to CD40 on a human APC by 16-88% and wherein said antibody synergistically enhances APC-mediated human CTL activation" (see claim 21)

"with an antibody or binding fragment thereof that binds to said receptor and blocks binding of CD40Lto CD40 by 16-88% (see claim 31);

"wherein said antibody or binding fragment thereof blocks binding of CD40L to CD40 by 16-25%" (see claim 32)

"an antibody in which the potential T cell epitopes have been eliminated" (see claim 24).

Applicant's amendment, filed 10/12/05, asserts that no new matter has been added and directs support to various pages and Examples / Figures of the instant specification for the written description for the above-mentioned "limitations".

However, the specification as filed does not provide sufficient written description as to the "above-mentioned limitations".

The recitation of "16-88%", "16-25%" and wherein said antibody synergistically enhances APC-mediated human CTL activation" is not readily apparent from applicant's specification as filed.

It appears that the recitation of "16-88%" and "16-25%" are drawn from the experimental observations from the disclosed CD40binding antibodies.

Also, it is noted that Example 2 on page 19 of the specification as filed discloses Table 1, however, there does not appear to be a Table 1 in the disclosure as filed.

Applicant is required to clarify the existence of Table 1 in the application as filed.

However, applicant's reliance on generic disclosure and possibly limited species does not provide sufficient direction and guidance to the "features" currently claimed.

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads.

See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

It is acknowledged that Example 5 of the instant specification discloses that certain CD40-binding antibodies that efficiently co-bind with sCD40L to its receptor will presumably show synergism with sCD40L or membrane bound CD40 in driving dendritic cell maturation or in the induction of IL-12p70 secretion as between as CTL activation between two different anti-CD40 antibodies.

However, the claims do not recite certain combinations of certain anti-CD40 antibodies with other certain anti-CD40 antibodies or sCD40L.

Rather the claims are limited to "an agonist anti-CD40 antibody or binding fragment thereof" and not combinations of certain anti-CD40 antibodies or anti-CD40 antibodies and CD40L.

Further, this disclosure of possible "synergism" in Example 5 appears to be prophetic statements, based upon certain anti-CD40 antibodies in combination with other certain anti-CD40 antibodies or sCD40L.

Again, applicant is claiming subgenera not supported by the specification as-filed.

None of these "above-mentioned limitations" are readily apparent in the specification as directed and neither does the context of the specification as these referenced sections of the instant specification provide sufficient blazemarks or direction for the instant methods encompassing the above-mentioned "limitations" drawn to subgenera, as currently recited.

With respect to the recitation of "an antibody in which the potential T cell epitopes have been eliminated", it is noted that this language is disclosed on page 8, paragraph 1 of the instant specification.

However, this disclosure is in the context of "Delmmunised antibodies" only.

Therefore, it appears that the current claims broaden the disclosure as filed.

Applicant is invited to clarify whether the disclosure as filed concerning "Delmmunised antibodies" is drawn to the products / antibodies themselves or the process by which the products / antibodies are made.

For example, if "Delmmunised antibodies" describes the process rather than the products per se, then this rejection may be obviated as applicant has disclosed "an antibody in which the potential T cell epitopes have been eliminated".

However, if "Delmmunised antibodies" describes particular characteristics such as particular potential T cell epitopes that are to be eliminated, then this rejection will stand.

Applicant is invited to clarify these issues.

The instant claims now recite "limitations" which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the limitations indicated above. See MPEP 714.02 and 2163.06.

6. Claims 21-24 and 29-30 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments, filed 10/12/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that co-administration of antigen is not a prerequisite to the treatment of compromised immune function and would enhance a weak CTL response mounted by the patient against the pathogen, including boosting a patient to achieve a properly activated immune system.

Applicant also relies upon the working example disclosed in the specification as filed that provides a well-recognized system in the art.

Applicant distinguishes the experiments in Melief et al. (US 2003/0022860) by asserting that the claimed methods are related to enhancing an immune response to any foreign antigen in an individual's system, rather that showing an enhancement to antigen to be tested against.

However, it appears that applicant's own Experiment 3 is consistent with the experiments in Melief et al. in that antigen was provided to show CTL activation and priming (e.g. see pages 21-22 of Example 3 in the instant specification).

Note, too, that the Background of the Invention of the instant specification discloses the well-known observations that "when they have not yet encountered their specific antigen, the immune system's T-killer cells (CTLs) circulate as inactive precursors" (e.g. see page 1 of the instant specification).

Further, Melief et al. teach that a CTL-activating peptide can become tolerogenic, meaning that the host reaction against cells expressing such peptide is inhibited, in the absence of anti-CD40 (e.g. see paragraph [0011]).

Applicant's arguments addressing those conditions boosting a weak immune response with the administration of anti-CD40 antibodies in the absence of antigen are not readily apparent in the disclosure of the instant application as filed and do not appear to be consistent with applicant's own Example 3 and the teachings of Melief et al.

Applicant's arguments are not found persuasive.

7. Applicant's amended claims, filed 10/12/05, have obviated the previous rejection under 35 U.S.C. § 112, second paragraph, with respect to the recitation of "DeImmunized".

8. Claims 21-24 and 30-32 are rejected under 35 U.S.C. § 102 (e) as being anticipated by Melief et al. (US 2003/0022860 A1; Jan. 30, 2003) (see entire document) essentially for the reasons of record.

Applicant's arguments, filed 10/12/05, have been fully considered but are not found convincing essentially for the reasons of record and those addressed herein.

Applicant argues that Melief et al. does not teach each and every element of the claims since the agonistic antibodies of Melief et al. differ substantially from the antibodies of the claimed invention.

However, applicant's arguments rely upon the exemplified anti-CD40 antibodies exemplified in Melief et al. and not upon the entire disclosure.

While the prior art FGK45 antibody recognizes mouse CD40 and the instant claims are drawn to human CD40, Melief et al. clearly is drawn to teaching treating humans by administering anti-human CD40 antibodies and certainly is not limited to administering only anti-mouse CD40 antibodies, as applicant appears to suggest.

For example, see paragraph [0029] of Melief et al. concerning making anti-human CD40 antibodies by well known techniques, as applicant has relied upon well known techniques to make anti-CD40 antibodies.

Applicant also argues that the agonist antibodies of the instant invention activate CD40 in addition to blocking CD40-CD40L interaction s by 16-88%, while the prior art FGK45 activates CD40 but does not block CD40 binding to CD40L, much less block binding of CD40 to CD40L by 16-88% as claimed.

Again, comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons.

In contrast to applicant's reliance upon a single antibody disclosed in the prior art, Melief et al. does teach agonistic anti-human CD40 antibodies which activate CTLs in combination with a CTL activating peptide (e.g. see paragraphs [0029] and [0035].

Although applicant asserts that the prior art anti-mouse CD40 antibody activates CD40 but does not block CD40 binding to CD40L, the evidence for this is not clear. Exhibit B concerning FGK45 does not appear to mention this inability to block CD40:CD40L binding at any level.

Again, Melief et al. teaches agonistic anti-human CD40 antibodies and does not teach agonistic anti-human CD40 antibodies that do not block CD40:CD40 interactions at any level.

Given the broad range of inhibition, including relatively low levels of inhibition (i.e. 16-88%), recited in the instant claims, the burden is on the applicant to establish a patentable distinction between the claimed and referenced agonistic anti-human CD40 antibodies, wherein said prior art anti-CD40 antibodies activate CTLs in combination with a CTL-activating peptides for treating humans.

Further, it is noted that the activity of biological materials can differ depending on assay conditions, such that "capable of blocking binding of CD40L on a human T lymphocyte to CD40 on a human APC by 16-88%" in one assay under one set of conditions, may not be the same in another assay or under different conditions.

As pointed out previously, Melief et al. teach methods of treating tumors or infectious diseases comprising administering anti-CD40 antibodies or fragments thereof, including monoclonal, chimeric, humanized, human, DEIMMUNISED and single chain antibodies (see paragraphs [0029] – [0034] and a CTL activating peptide by generating or enhancing immune responses via the CD40 pathway on dendritic cells. (see Background of the Invention, Summary of the Invention, and Making and Using the Invention).

Applicant's arguments have not been found persuasive.

9. Claims 21-24 and 30-32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Melief et al. (US 2003/0022860 A1; Jan. 30, 2003) in view of Zhou et al. (Hybridoma 18: 471 - 478, 1999) (of record) AND/OR Caux et al. (Research in Immunology 145: 235-239, 1994) (of record) AND/OR Katira et al. (Leukocyte Typing V, Schlossman et al. (Ed.), Oxford University Press, Oxford 1995, page 554) (of record) AND/OR Schwabe et al. (Hybridoma 16 : 217 – 226, 1997) (of record)) essentially for the reasons of record.

Claim 29 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Melief et al. (US 2003/0022860 A1; Jan. 30, 2003) in view of Zhou et al. (Hybridoma 18: 471 - 478, 1999) AND/OR Caux et al. (Research in Immunology 145: 235-239, 1994) AND/OR Katira et al. (Leukocyte Typing V, Schlossman et al. (Ed.), Oxford University Press, Oxford 1995, page 554) AND/OR Schwabe et al. (Hybridoma 16 : 217 – 226, 1997)
as applied to claims 21- 24 and 30-32 above and further in view of Maraskovsky et al. (U.S. Patent No. 6,497,876)) essentially for the reasons of record.

Applicant's arguments, filed 10/12/05, have been fully considered but are not found convincing essentially for the reasons of record and those addressed herein.

Applicant's arguments and the examiner's rebuttal are essentially the same as those addressed above in the previous Section 8.

Again, Melief et al. teaches agonistic anti-human CD40 antibodies and does not teach agonistic anti-human CD40 antibodies that do not block CD40:CD40 interactions at any level.

Similarly there is insufficient objective evidence that the prior art agonistic anti-human CD40 antibodies would not block CD40:CD40L interactions on a human T lymphocyte, given the broad range of inhibition, including relatively low levels of inhibition (i.e. 16-88%), recited in the instant claims and differences in activities based upon differences in assays and assay conditions.

For example, Schwabe et al. does teach anti-CD40 agonistic antibodies with antibodies that define an epitope that was congruent with the CD40L binding site (e.g. see Abstract).

While Katira et al. do describe antibodies of a particular subgroup that do not block CD40:CD40L interactions, this property appears to be limited to certain anti-CD40 antibodies and not to all of the agonistic anti-CD40 antibodies described.

Given the broad range of inhibition, including relatively low levels of inhibition (i.e. 16-88%), recited in the instant claims, the burden is on the applicant to establish a patentable distinction between the claimed and referenced agonistic anti-human CD40 antibodies, wherein said prior art anti-CD40 antibodies activate CTLs in combination with a CTL-activating peptides for treating humans.

Further, it is noted that the activity of biological materials can differ depending on assay conditions, such that "capable of blocking binding of CD40L on a human T lymphocyte to CD40 on a human APC by 16-88%" in one assay under one set of conditions, may not be the same in another assay or under different conditions.

Again, once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather merely asserts that the prior art does not provide sufficient suggestion or motivation to enhance immune responses with agonistic antibodies and does not address the teachings of the references individually and not their teachings individually or in combination.

One cannot show non-obviousness by merely asserting that the references do not provide the sufficient elements of obviousness or by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

In addition, the arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01 (C). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results.

Applicant's arguments have not been found persuasive.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, Ph.D., J.D.
Primary Examiner
Technology Center 1600
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